REMARKS

In the Office Action issued June 13, 2003, the Examiner stated that pending claims 1-26 were rejected. The Examiner is reminded that claims 11 and 19 were cancelled in the Amendment filed April 7, 2003. Accordingly, claims 1-10, 12-18 and 20-26 were pending upon entry of the April 7, 2003 Amendment. In response to the June 13, 2003 Office Action, claims 1, 17 and 26 have been amended and claim 10 has been cancelled. Upon entry of this amendment, claims 1-9, 12-18 and 20-26 remain pending for the Examiner's consideration. Withdrawal of the previous rejections under Section 112, first and second paragraph, is acknowledged. Reexamination and reconsideration of the application, as amended, are requested.

Rejections under 35 U.S.C. § 103(a) addressed

1. Claims 1-6, 9-14, 16-23, and 25-26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Yu et al. (5,385,938) in view of Poli et al. (Food Chemistry), Wenniger (International Cosmetic Ingredient Dictionary), and the Merck Index. This rejection is respectfully traversed.

Independent claim 1 as amended herein is directed to a method for the prophylaxis of lesions in a mammal caused by a virus of the Herpesviridae or Poxviridae family, comprising topically applying a composition consisting essentially of

> a synergistic combination, said combination consisting of a C1, a C2, or a C3 alcohol or a C2, C3, or C4 diol having a concentration of 0.2 to 13.0% by volume in water, and a sufficient amount of an acid to adjust the pH of the synergistic combination to between 2.45 and 4.6.

It is well known that the transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps and those that do not materially affect the basic and novel characteristic(s) of the claimed invention. Accordingly, the transitional phrase "consisting essentially of" requires that the composition contains a synergistic composition as set forth in claim 1, but excludes active agents other than the synergistic combination of the alcohol and acid.

Further, the phrase "consisting of" in claim 1 clearly indicates that the synergistic combination contains only:

- a C1-C3 alcohol or a C2-C4 diol having a concentration of 0.2 to 13.0% by volume in water, and
- a sufficient amount of an acid to adjust the pH of the synergistic combination to between 2.45 and 4.6.

Accordingly, any element or ingredient other than a C1-C3 alcohol or a C2-C4 diol having a concentration of 0.2 to 13.0% by volume in water and a sufficient amount of an acid to adjust the pH of the synergistic combination to between 2.45 and 4.6 is excluded from the synergistic combination of claim 1. Independent claims 17 and 26 have been amended in a manner similar to that of claim 1 and therefore the above remarks apply equally to claims 17 and 26.

In contrast, Yu teaches a first example of composition containing two agents: an alpha hydroxyacid or alpha ketoacid and an amphoteric or pseudoamphoteric compound. The amphoteric or pseudoamphoteric compound is intentionally added to raise the pH of the composition in order to avoid skin irritation (see column 4, lines 2-12). Specifically, Yu states that a 1 molar aqueous solution of glycolic acid has a pH of 1.9, but the pH of the composition changes to 3.0 or 3.2 when an amphoteric compound such as arginine or creatinine, respectively, is combined with the glycolic acid solution. Thus, in this example Yu's active composition requires both an alpha hydroxyacid and an amphoteric compound. Therefore Yu's composition contains an element, i.e., an amphoteric compound, which is specifically excluded from the elements allowed in the synergistic combination of claims 1-6, 9-14, 16-23, and 25-26.

Yu also describes a formulation containing specific alpha hydroxy acids which are therapeutically effective for certain skin disorders without utilizing an amphoteric system (column 11, line 55-column 12, line 2), and provides glycolic acid as an example of an effective alpha hydroxy acid. However, as discussed above, the pH of a glycolic acid solution that does not include an amphoteric compound is **1.9**, which is outside of the pH range of 2.45 to 4.6 as required in claim 1. Accordingly, this alternative composition disclosed by Yu is also outside of the scope of claims 1-6, 9-14, 16-23, and 25-26 as presently pending.

Therefore, since Yu does not teach or even suggest every element of the composition of claims 1-6, 9-14, 16-23, and 25-26, Yu cannot render claims 1-6, 9-14, 16-23, and 25-26 obvious.

Next, the Examiner asserts that Yu does not expressly teach that the glycolic acid is useful in the prophylaxis of lesions caused by viruses within the Herpesvirdae family, and

relies on Poli for teaching that glycolic acid is virucidal against herpesvirus. Poli describes a study to determine the *in vitro* antiviral activity of certain organic acids. Poli found that certain organic acids have antiviral activity, and that this activity was found to be proportional to the polarity of the molecule (page 255, last paragraph). However, Poli does not teach or even suggest that the pH of the acid solution is critical for virucidal activity. Further, Poli does not teach or even suggest a method of preventing a lesion caused by a virus using a composition consisting essentially of a synergistic combination consisting of a low concentration of a lower chain alcohol and an acid at a specific pH. Thus, even if there were a motivation to combine the acids disclosed by Poli with the Yu composition, such a combination would not teach the methods of the present invention.

Next, the Examiner asserts that while Yu does not expressly teach that 1,3-butanediol is useful as a pharmaceutical vehicle, Wenniger teaches that 1,3-butanediol is useful as a solvent in numerous cosmetic marketed products. However, it is asserted that the Wenniger reference adds nothing to Yu that would render claims 1-6 and 9-14, 16-23 and 25-26 obvious. Even if there were a motivation to combine the references, the combination would not provide a method of treating an inflammation or lesion caused by a virus by contacting the inflammation or lesion with a composition **consisting essentially of** a synergistic combination, said synergistic combination **consisting of** a C1-C3 alcohol or a C2-C4 diol having a concentration of 0.2 to 13.0% by volume in water, and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6.

Finally, the Examiner asserts that while Yu does not expressly teach the composition having a specific pH of 2.45 and does not teach the concentration of glycolic acid in the composition as 0.6%, the Merck Index teaches that the pH of a 0.5% glycolic acid is 2.50. However, it is asserted that the Examiner's inclusion of the Merck Index adds nothing to the above combination of references that would render claims 1-6 and 9-14, 16-23 and 25-26 obvious. As stated, the novel feature of the present invention is the synergistic combination **consisting of** a C1-C3 alcohol or a C2-C4 diol having a concentration of 0.2 to 13.0% by volume in water, and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6. That is, the inventors discovered that this novel synergistic combination can be used to prevent the formation of lesions caused by a virus when applied topically to the potential site of a lesion. Thus, the Examiner's use of the Merck Index citation is weak at best and shows that the Examiner clearly is not considering the invention as a whole.

In summary, even if there were motivation to combine the above references, the combination still would not provide the novel methods of claims 1-6 and 9-14, 16-23 and 25-26 as amended herein. Withdrawal of this rejection is respectfully requested.

2. Claims 1, 7-8, 15 and 24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bhatia et al. (Indian J. Animal Sci.) in view of Disinfectant Drugs (Therapeutic Products Programme Guidlelines) and Remington (Remington's Pharm. Sci.).

The Examiner asserts that Bhatia teaches that 0.4N hydrochloric acid is effective in inactivating sheep pox virus, but does not expressly teach the use of hydrochloric acid with an alcohol in the amount of 0.2 to 30%, or 0.2% to 12.5% in volume. The Examiner then asserts that Disinfectant Drugs teaches that isopropanol 15% or above is effective as a single medicinal ingredient for disinfecting contact lenses. This rejection is respectfully traversed, in part because Disinfectant Drugs constitutes non-analogous art.

To qualify as analogous prior art, a reference "must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oetiker*, 977 F.2d 1443, 1446 (Fed. Cir. 1992). "A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's filed of endeavor, is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem." *In re Clay*, 966 F.2d 656, 659 (Fed. Cir. 1992).

The field of endeavor of the present case relates to includes:

> virucidal compositions for the treatment and/or prevention of superficial lesions or sores, including canker sores and lesions caused by viruses of the Herpesviridae and Poxviridae families.

(Specification, paragraph [0002]. The particular problem with which the inventors were concerned is that

> [w]hile there are now large numbers of compounds that have been found to exhibit antiviral activity against cold viruses in cell culture, many antiviral compounds have had limited effectiveness in patients. [Thus, a] need continues to exist for topical compositions that are active against enveloped and naked viruses and have very low toxicity.

(Specification, paragraphs [0007] and [0021].

In contrast, Disinfecting Drugs is titled "Contact Lens Disinfectants" and more specifically provides products in liquid or tablet form to be used to disinfect contact lenses. Contact lens disinfectants are clearly not within the Applicants' field of endeavor.

Thus the question becomes, what is the problem with which Disinfecting Drugs is concerned and is it reasonably pertinent to for the prophylaxis of lesions in a mammal caused by a virus of the Herpesviridae or Poxviridae family? Upon reviewing Disinfecting Drugs, it is clear that there is no particular problem with which Disinfecting Drugs is concerned. Rather, Disinfecting Drugs is a simple monograph describing the protocols for cleaning contact lenses, and lists acceptable single and combination medicinal ingredients. Disinfecting Drugs lists isopropyl alcohol at 15% concentration as an acceptable single ingredient, but does not provide isopropyl alcohol in combination with any other ingredients (page 43). Accordingly, Disinfecting Drugs is not reasonably pertinent to the problem with which the inventors in the present case were concerned — the prophylaxis of lesions in a mammal caused by a virus of the Herpesviridae or Poxviridae family. As a result, under the 2-part test established by the Federal Circuit, Disinfecting Drugs constitutes non-analogous art relative to the present invention and cannot be used as a basis for rejection of the claims now pending in the present application. Because the Office Action relies on both cited references for its obviousness rejection of pending claims 1, 7-8, 15 and 24, without Disinfecting Drugs, *prima facie* obviousness cannot be maintained by the combination with Bhatia. Accordingly, withdrawal of the obviousness rejection of claims 1, 7-8, 15 and 24 is respectfully requested.

Further, even if Disinfecting Drugs was a proper prior art reference, it is asserted that Bhatia in combination with Disinfecting Drugs does not teach or suggest the methods of the present invention. The purpose of Bhatia was to determine if hydrochloric acid would inactivate the goat-pox virus *in vitro* **prior** to contacting the acid with the goats' skin. Bhatia discloses a method of combining goat-pox virus with hydrochloric acid and incubating this suspension for a period of time (see page 518, second column, last paragraph). In order to determine if the virus was still active after incubation with acid, Bhatia injected the suspension under the goats' skin and watched for signs of pain at the injection site.

Thus, the Bhatia composition is actually a mixture of the goat-pox virus and a concentrated acid. Further, Bhatia only demonstrates that acid kills a virus *in vitro*. Bhatia does not teach or even suggest applying acid to the skin to prevent an inflammation or lesion caused by a virus of the Herpesviridae or Poxviridae family. More importantly, Bhatia does

not teach or even suggest a method of preventing an inflammation or lesion caused by a virus by applying to the inflammation or lesion a composition consisting essentially of a synergistic composition, wherein the synergistic composition consists of a C1-C3 alcohol or C2-C4 diol and an acid having a concentration of 0.2-13% by volume of, wherein the pH of the mixture is between 2.45 and 4.6. Accordingly, even if there were a motivation to combine the teachings of Bhatia with the teachings of Disinfecting Drugs, the combination would not render the methods of this invention obvious. Withdrawal of this rejection is respectfully requested.

CONCLUSIONS

All of the remarks in the final Office Action have been addressed, claims 1-9, 12-18, and 20-26 are believed to be in condition for allowance, and such action is respectfully requested. The fee for filing a Petition for a three month time extension is included with this response. Should any additional fees be due, the Examiner is authorized to charge any fee deficiency associated with this response to Deposit Account No. 50-1123. The Examiner is asked to kindly contact the undersigned by telephone should any outstanding issues remain.

Respectfully submitted,

Dated: Dec. 15, 2003

Sarah O'Rourke, Reg. No. 41,226
Hogan & Hartson, L.L.P.
1200 Seventeenth Street, Suite 1500
Denver, Colorado 80202
Telephone: (720) 406-5385
Facsimile: (720) 406-5301